

anticipated by Bahl et al. (Oncogene, 1/2000) ("Bahl"); and claims 2-7 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ralhan et al. (Clinical Cancer Research, 7/2000) ("Ralhan").

In view of the amendments and remarks herein, Applicant respectfully requests reconsideration and withdrawal of the rejections set forth in the Office Action.

I. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 2-7 and 13-16 are rejected under 35 U.S.C. §112, first paragraph.

According to the Office Action, the specification:

While being enabling for a method for screening subjects in the Indian, human population having or at risk of having esophageal cancer by PCR amplifying DNA isolated from either a blood, normal tissue or tumor tissue sample and assaying for the presence of the A to G polymorphism at codon 149 of the p21 waf1/cip1 gene does not reasonably provide enablement for a method for screening any subject from anywhere having or at risk of having esophageal cancer by PCR amplifying DNA isolated from any specimen or methods for genotyping cancer patients for the p21 waf1/cip1 codon 149 variant as a predictor of radiosensitivity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 2, 13 and 14 have been amended to limit the tested subjects to humans. In addition, these claims have been amended to limit the cancer to esophageal cancer.

With respect to the issue of whether the claims should be limited to Indians, Applicant submits that the instant specification does not teach or suggest such a limitation. The invention is directed to a method for screening subjects having or at risk of having esophageal cancer by detecting polymorphism in p21^{waf1/cip1} gene. The method of the invention can be used to detect a polymorphism in the p21^{waf1/cip1} gene in

anyone who exhibits such polymorphism. The specification does not teach or suggest that only those who are Indian will have such a polymorphism. Although Indians, because of their diet, may have a higher chance of exhibiting this particular polymorphic variant, non-Indians may also exhibit such polymorphism.

Bahl teaches that:

Shows side geographical variation in incidence across the world, with a strong correlation with exogenous risk factors, namely, alcohol consumption and tobacco smoking in Western countries, and a variety of dietary factors confounded by nutritional deficiency in several regions of India and China The etiology of Esophageal Squamous Cell Carcinoma (ESCC) is multifactorial, with synergetic effect of environmental and dietary factors. High consumption of sun dried and pickled vegetables, red chillies, and spices in the Indian population are implicated as major predisposing factors to esophageal tumorigenesis In addition, bidi smoking, pan chewing and pan-tobacco chewing have also been identified as important risk factors for esophageal cancer in India **The Indian population, with poor nutritional status and high exposure to these dietary risk factors may therefore serve as an important *in vivo* model** to investigate the alterations in oncogenes and tumor suppressor genes implicated in the pathogenesis of EC, which may ultimately lead to the identification of novel predisposing factors or molecular markers for early diagnosis. [emphasis added]

Thus, Bahl teaches that Indians, because of their high exposure to certain dietary risk factors, may serve as models to study but this teaching does not indicate that only Indians can possess the polymorphic variant in question or that only Indians can undergo screening for the polymorphic variant.

With respect to the issue of whether the claim should be limited to state that the DNA is isolated from blood, normal tissue or tumor tissue sample, Applicant respectfully submits that the source of the DNA does not affect the outcome of the claimed method so long as the DNA is taken from the subject being tested. It is the

DNA itself which is important, not which part of the subject's body the DNA sample originates.

For these reasons, Applicant respectfully requests that the rejection under § 112, first paragraph, be withdrawn.

II. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 2-7 and 13-16 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

According to the invention, there is lack of antecedent basis for the recitation "codon 149, GAT to GGT transition, ... the codon 149 polymorphic variant". The Office Action states that the claims should be amended to consistently term the event at codon 149 as a transition to provide adequate antecedent basis. Claims 2, 13 and 14 have been amended as suggested by the Examiner.

Claims 2-7 are also to be indefinite because claim 2 is drawn to a method of screening subjects having or at risk of having esophageal cancer, whereas the final process step is directed to detecting an SNP indicative of risk of cancer. According to the Office Action, it is unclear whether the claim is intended to be limited to methods of screening subjects having or at risk of having esophageal cancer or just for detecting an SNP indicative of risk of cancer as referred to in the preamble.

The preamble of claim 2 has been amended herein to state that the method is for detecting a single nucleotide polymorphism in human subjects having or at risk of having esophageal cancer and that the polymorphism is indicative of risk of esophageal cancer.

Claims 13-16 are also to be indefinite because claim 13 is drawn to a method of genotyping cancer patients as a predictor of radiosensitivity of tumors, whereas the final process step is directed to detecting an SNP indicative of risk of cancer. According to the Office Action, it is unclear whether the claim is intended to be limited to methods

for genotyping cancer patients as a predictor of radiosensitivity of tumors or just for detecting an SNP indicative of risk of cancer as referred to in the preamble.

The preambles of claims 13 and 14 have been amended to state that the method is for detecting a p21^{waf1/cip1} codon 149 polymorphic variant in human cancer patients. The claim 13 preamble further states that the variant is a predictor of radiosensitivity of tumors.

In view of the amendments to claims 2, 13 and 14, Applicant respectfully requests that the rejection under §112, second paragraph, be withdrawn.

III. Rejection Under 35 U.S.C. §102(a)

Claims 2-7 are rejected under 35 U.S.C. §102(a) as being anticipated by Bahl. Applicant submits herewith a Katz-type “Declaration Under 37 CFR 1.132”, wherein Applicant declares that he is the sole inventor of the subject matter described and claimed in the instant application and of the subject matter described in the Bahl publication and that the other authors of the Bahl publication are not co-inventors.

Applicant respectfully submits that the Declaration overcomes the §102(a) rejection.

IV. Rejection Under 35 U.S.C. §103(a)

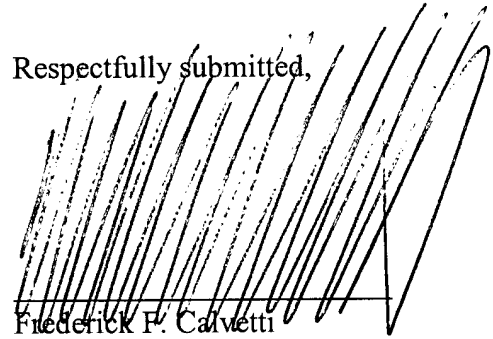
Claims 2-7 are rejected under 35 U.S.C. §103(a) as being anticipated by the Ralhan. Applicant submits herewith a Katz-type “Declaration Under 37 CFR 1.132”, wherein Applicant declares that he is the sole inventor of the subject matter described and claimed in the instant application and of the subject matter described in the Ralhan publication and that the other authors of the Ralhan publication are not co-inventors.

Applicant respectfully submits that the Declaration overcomes the § 103(a) rejection.

V. Conclusion

In view of the foregoing amendments and remarks and the enclosed Declarations, Applicant respectfully requests that the rejections set forth in the Office Action be withdrawn and that claims 2-7 and 13-16 be allowed.

Respectfully submitted,

A large, stylized handwritten signature in black ink, consisting of many overlapping, sweeping strokes that form a dense, somewhat abstract shape.

Frederick P. Calvetti
Reg. No.28,557

Date : February 5, 2003

SMITH, GAMBRELL & RUSSELL
1850 M Street, N.W., Suite 800
Washington, D.C. 20036
Telephone: (202) 973-2628
Facsimile: (202) 263-4329

Enclosures: Two Declarations Under 37 CFR 1.132

MARKED-UP PREVIOUS VERSION OF AMENDED CLAIMS

2. (Amended) A method for [screening of] detecting a single nucleotide polymorphism in human subjects having or at risk of having esophageal cancer, said polymorphism being indicative of risk of esophageal cancer, the method comprising:

- a) amplifying a target nuclei acid in DNA isolated from a specimen of a subject;
- b) purifying the PCR products;
- c) DNA sequencing of the PCR products;
- d) detecting single nucleotide polymorphism in p21^{waf1/cip1} gene by determining codon 149, GAT→GGT transition, or by observing the presence or absence of the codon 149 [polymorphic variant] transition, wherein the transition is a polymorphism that [, further wherein the presence of the polymorphism] is indicative of risk of esophageal cancer.

13. (Amended) A method for [genotyping] detecting a p21^{waf1/cip1} codon 149 polymorphic variant in human cancer patients, [for] said p21^{waf1/cip1} codon 149 variant [as] being a predictor of radiosensitivity of tumors, said method comprising:

- a) amplifying a target nuclei acid in DNA isolated from a specimen of a human subject by polymerase chain reaction (PCR) using specific oligonucleotide primers;
- b) purifying the PCR products;
- c) DNA sequencing of the PCR products; and
- d) detecting single nucleotide polymorphism in p21^{waf1/cip1} gene by determining codon 149, GAT→GGT transition, or by observing the presence or absence of the codon 149 [polymorphic variant] transition, wherein the transition is a [presence of the] polymorphism that is indicative of risk of cancer.

14. (Amended) A method for [genotyping] detecting a p21^{waf1/cip1} codon 149 polymorphic variant in human cancer patients [for p21^{waf1/cip1} codon 149] using the method according to claim 2 for designing cancer treatment protocols.